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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/689,730	10/13/2000	Motoharu Seiki	0055-0310P	6821

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BIRCH STEWART KOLASCH & BIRCH
PO BOX 747
FALLS CHURCH, VA 22040-0747

EXAMINER
PROUTY, REBECCA E

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 06/17/2003

12

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/689,730	Seiki et al.
Examiner	**Art Unit**
Rebecca Prouty	1652

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Apr 3, 2003* .

2a) ☒ This action is **FINAL.** 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *13-15 and 23-26* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☒ Claim(s) *24 and 25* is/are allowed.

6) ☒ Claim(s) *13-15, 23, and 26* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

Claims 1-12 and 16-22 have been canceled. Claims 13-15 and newly presented claims 23-26 are still at issue and are present for examination.

Applicants' arguments filed on 4-3-03, paper No. 11, have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because: the oath claims foreign priority under 35 U.S.C. 119 to international application PCT/JP94/02009 yet applicants letter of 10-13-00 indicates that applicants intend the instant application to be a divisional of 08/448,489 which is a CIP of the international application under 35 U.S.C. 120 and 365(c).

The amendment filed 10-13-00 is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The objection is explained in the previous Office Action.

Applicants argue that it is well established that there does not have to be *ipsis verbis* support in the specification and that what is necessary is that one of skill in the art would recognize upon reading the specification that the new language reflects what the specification shows has been invented. This is acknowledged but is **exactly** the problem in the instant case. One of skill in the art reading the specification as filed would **not** have recognized that applicants considered polyclonal antibodies to be part of their invention because in every instance in which antibodies were discussed, the specification specifically said monoclonal antibodies. As such the skilled artisan would have believed that applicants considered the invention to be limited to monoclonal antibodies only. The portions of Example 3 that produce polyclonal antibodies are clearly disclosed only as intermediate steps in obtaining the monoclonal antibodies of the invention.

Applicant is required to cancel the new matter in the reply to this Office Action.

Claims 13-15, 23 and 26 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s),

at the time the application was filed, had possession of the claimed invention.

Claims 13 and 23 are directed to a genus of nucleic acids encoding a polypeptide having metalloproteinase activity and comprising amino acids 160-173 (or 1-173), 320-333, 498-512, and 533-562 of SEQ ID NO:1. Claim 26 is drawn to any polynucleotide which will hybridize to SEQ ID NO:2 under stringent conditions. The specification does not contain any disclosure of the structure of all nucleic acid sequences included in the claimed genera of Claims 13 and 23 nor the function of all nucleic acids within the scope of Claim 26. The genera of nucleic acids claimed is a large variable genus with including many structurally or functionally different polynucleotides. Many structurally distinct nucleic acids are encompassed within the scope of claims 13 and 23 and many functionally distinct nucleic acids are encompassed within the scope of claim 26. The specification discloses only a single species of the claimed genera (i.e., that of SEQ ID NO:2) which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genera. The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings,

or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus, A representative number of species means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. Satisfactory disclosure of a representative number depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed. For inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus. A sufficient written description of a genus of DNAs may be achieved by a recitation of a representative number of DNAs defined by nucleotide sequence or a recitation of structural features common to members of the genus, **which features**

constitute a substantial portion of the genus. The recited structural feature of the genus (i.e., encode a polypeptide comprising several fragments of SEQ ID NO:1) does not constitute a substantial portion of the genus as the remainder of the structure of any nucleic acid encoding a polypeptide having metalloproteinase activity is completely undefined and the specification does not define the remaining structural features necessary for members of the genus to be selected. For Claim 26, the claim genera includes species which are widely variant in function. The genus Claim 26 is functionally diverse as it encompasses polynucleotides encoding polypeptides with metalloproteinase activity, those which lack such activity but are capable of use as probes and polynucleotides with neither of these utilities but possibly other uses. As such, neither the description of the structure and function of SEQ ID NOS:2 nor the disclosure solely structural features present in all members of the genus is sufficient to be representative of the attributes and features of the entire genus.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claims 13-15, 23, and 26 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for polynucleotides encoding a membrane-type matrix metalloproteinase which will hybridize to SEQ ID NO:2 under stringent conditions as recited in Claim 26, does not reasonably provide enablement for any polynucleotide encoding a membrane-type matrix metalloproteinase comprising amino acids 160-173 (or 1-173), 320-333, 498-512, and 533-562 of SEQ ID NO:1 or any polynucleotide which will hybridize to SEQ ID NO:2 under stringent conditions. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Claim 13 and 23 are so broad as to encompass any membrane-type matrix metalloproteinase comprising amino acids 160-173 (or 1-173), 320-333, 498-512, and 533-562 of SEQ ID NO:1. Claim 26 is drawn to any polynucleotide which will hybridize to SEQ ID NO:2 under stringent conditions. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of polynucleotides broadly encompassed by the claims. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's

amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to a single polynucleotide encoding a membrane-type matrix metalloproteinase and an alignment of the amino acid sequence encoded thereby with the sequence of several known matrix metalloproteinases.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass any polynucleotide encoding a membrane-

type matrix metalloproteinase comprising amino acids 160-173 (or 1-173), 320-333, 498-512, and 533-562 of SEQ ID NO:1 or any polynucleotide which will hybridize to SEQ ID NO:2 under stringent conditions because the specification does **not** establish: (A) regions of the protein structure which may be modified without effecting metalloproteinase activity; (B) the general tolerance of metalloproteinases to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any metalloproteinase residues with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any polynucleotide encoding a membrane-type matrix metalloproteinase comprising amino acids 160-173 (or 1-173), 320-333, 498-512, and 533-562 of SEQ ID NO:1 or any polynucleotide which will hybridize to SEQ ID NO:2 under stringent conditions. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient

guidance, determination of polynucleotides having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claims 24 and 25 are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rebecca Prouty, Ph.D. whose telephone number is (703) 308-4000. The examiner can normally be reached on Monday-Friday from 8:30 to 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy, can be reached at (703) 308-3804. The fax phone number for this Group is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Rebecca Prouty
Primary Examiner
Art Unit 1652